Bandolier

What do we think? What do we know? What can we prove? 38

Evidence-based health care

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Don't squirrel knowledge

Bandolier was shocked recently to hear of readers who kept the information in our pages to themselves. Squirreling away information isn't the point of all this. Knowledge is to be shared, discussed, argued over, and, sometimes, acted upon.



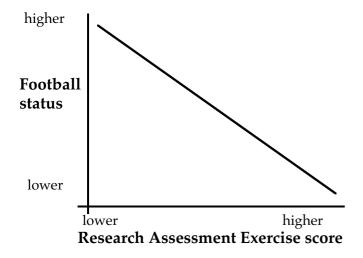
Treating information as a surrogate for power is all to do

with organisational attitude and size. Most small organisations share information because there is a mutual imperative to grow and excel - knowledge empowers everyone. Large organisations become more bureaucratic - more secretive - and the bad squirrels take over.

So organisations that want to tackle change effectively need an anti-squirrel campaigner to turn over these bad habits. Ask yourself whether your organisation has a "Chief Knowledge Officer" squirrel warden. Make a start yourself - share your *Bandolier* with a colleague!

Don Cantona

Our Indoor Games Editor is perplexed by the apparent relationship between scores achieved by the various clinical schools on the Research Assessment Exercise (RAE) and the achievement of the football team in the respective conurbation. It is an inverse relationship. High scores on the RAE are associated with relatively lowly status football, and low RAE scores with premier league football. Matching football team and clinical school in London will cause great uproar.



Of course, this may just be another example of 'all that correlates isn't meaningful'. How often we see that in papers we read.

But if this particular correlation is meaningful, the cure in a free market economy must lie in the transfer market. Prizes for sightings of medical school deans in motorway service station negotiations.

Snoring Sunset

Clinical industries can rise rapidly from the primordial slime of ignorance. Two reviews [1, 2] and an editorial [3] should make us think twice about whether obstructive sleep apnoea is a real problem, even if cures exist. In the review from the NHS Centre for Reviews at York [1], there is an amazing quote from the New England Journal of Medicine "sleep apnoea may be as big a public health hazard as smoking".

The York team debunk this hyperbole. They conclude "the relevance of sleep apnoea to public health has been exaggerated", and they believe that the continuous positive airways pressure cure has been poorly evaluated. Tough, and important reading.

References:

- 1 J Wright, R Johns, I Watt, A Melville, T Sheldon. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airways pressure. British Medical Journal 1997 314: 851-60.
- 2 MM Ohayon, C Guilleminault, RG Priest, M Caulet. Snoring and breathing pauses during sleep: telephone interview survey of a United Kingdom population sample. British Medical Journal 1997 314: 860-3.
- 3 JA Fleetham. A wake-up call for sleep disordered breathing (editorial). British Medical Journal 1997 314: 839-40.

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The views expressed in Bandolier are those of the authors, and are
not necessarily those of the NHSE Anolia & Oxford

NNTs for stroke prevention

Bandolier 17 carried a table of NNTs (numbers needed to treat) for cardiac interventions. People seemed to like this gathering together of information, though it isn't easy work. This month we have gathered together some information on NNTs for stroke prevention calculated from randomised trials of primary and secondary prevention.

NNT table

For NNTs to be comprehensive and comprehensible you have to know the population studied, their disease and its severity, the treatment, the comparator, and the duration of treatment as well as the outcome. So the table *Bandolier* offers has this information.

Outcomes

The outcome we chose to extract from papers was total strokes - that is all non-fatal and fatal strokes. Some papers offered transient ischaemic attack (TIA) as well, but we chose not to include this. Only comparisons with placebo are offered, without any discrimination for particular drug treatment, either because it was not given in the original paper or because there was no difference except for one study [9].

The numbers of events which occurred over the study period were taken as the numerator. The denominator was the number of patients originally randomised. Because some of these studies included or concentrated on elderly people, after some years the numbers of people still in the study had fallen. So this form of analysis may give slightly different estimates from those in the original papers which used different methods. The table provides relative risk and NNTs with 95% confidence intervals. The order of papers is chronological.

Results

Primary prevention

Two studies of antihypertensive treatment in hypertensive people over 60 years [3,4] have NNTs of about 40 to prevent one stroke over 4 years compared with placebo. This means that 40 people have to be treated for four years to prevent a stroke in one of them, who would have had a stroke if they had been given a placebo. The confidence intervals were wide, though.

The MRC study of treatment of hypertension in older adults [6] concluded that there was a significant reduction in strokes (101/2183 treated patients compared with 134/2213 with placebo). Differences became really apparent after 4 years, and the NNT was 70.

These results for single trials have to be compared with the overall NNT of 43 (31 - 69) over five years found in a metaanalysis of hypertension treatment in the elderly (*Bandolier* 15, [10]).

Secondary prevention

One of the secondary prevention studies [7] was designed to assess the effectiveness of cholesterol lowering. It did, however, show a benefit in reducing strokes, with a NNT of 65.

Three studies examining treatments in patients who had already had a stroke or TIA had lower (better) NNTs. Lowdose aspirin (75 mg) over a mean of 2.7 years had an NNT of 38 [5]. Ticlopidine over two years had an NNT of 15 [2]. Very low dose aspirin (25 mg) or dipyridamole alone had an NNT of about 40 over two years, but the effects were additive with a two-year NNT of 18 for the combined treatment [9].

Comment

People have to make their own minds up about the value of these treatments. They also have to remember that the NNT refers to a time period, and that it is probably not quite legitimate to "normalise" the NNTs by multiplying by the time period to get NNTs/year.

Nevertheless, knowing that there are treatments which prevent another stroke occurring, in a patient who has already had one, with NNTs of below 20 for two years, is encouraging.

References:

- MRC trial of treatment of mild hypertension: principal results. British Medical Journal 1985 291: 97-104.
- 2 M Gent et al. The Canadian American ticlopidine study (CATS) in thromboembolic stroke. Lancet 1989 i: 1215-20
- 3 Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Journal of the American Medical Association 1991 265: 3255-64.
- 4 B Dahlöf et al. Morbidity and mortality in the Swedish trial in old patients with hypertension (STOP-hypertension). Lancet 1991 338:1281-5.
- 5 Swedish aspirin low-dose trial (SALT) of 75 mg aspirin as secondary prophylaxis after cerebrovascular ischaemic events. Lancet 1991 338:1345-9.
- MRC trial of treatment of hypertension in older adults: principal results. British Medical Journal 1992 304:405-12.
- 7 Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian simvastatin survival study (4S). Lancet 1994 344: 1383-9
- 8 J Shepherd et al. Prevention of coronary heart disease with privastatin in men with hypercholesterolaemia. New England Journal of Medicine 1995 333:1301-7.
- 9 HC Diener et al. European stroke prevention study 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. Journal of Neurological Sciences 1996 143: 1-13.
- 10 CD Mulrow et al. Hypertension in the elderly. Implications and generalizability of randomized trials. Journal of the American Medical Association 1994 272: 1932-8.

Randomised trials with outcome of total stroke (excluding TIA)

Study	Population	Treatments	Period	Relative risk	NNT
Primary prevention				(compared	with placebo)
MRC [1]	17,354 individuals 36-64 years diastolic 90-109 mmHg	benzoflurazide propranolol placebo	5.5 years		850 to prevent one stroke at one year
SHEP [3]	4736 individuals 60 years or older systolic 160-219 mmHg and diastolic <90 mmHg	clorthalidone atenolol placebo	4.5 years	0.65 (0.51 - 0.83)	43 (27 - 95)
STOP [4]	1627 individuals 70-84 years systolic 180-230 mmHg and diastolic ≥90 mmHg or diastolic 105-120 mmHg	atenolol hydrochlorothiazide plus amiloride metoprolol pindolol placebo	4 years	0.55 (0.30 - 0.97)	34 (20 - 123)
MRC [6]	4396 individuals 65-74 years systolic 160-209 mmHg diastolic <115 mmHg	diuretic ß-blocker placebo	5.8 years	0.76 (0.59 - 0.98)	70 (36 - 997)
WOSCOPS [8]	6595 men 45-64 years cholesterol over 6.5 mmol/L	privastatin placebo	4.9 years	0.90 (0.61 - 1.34)	641 (135 - no benefit)
Secondary prev	vention				
CATS [2]	1072 patients 1 week to 4 months after stroke	ticlopidine placebo	2 years	0.61 (0.44 - 0.84)	15 (9 - 41)
SALT [5]	1360 patients 50-79 years TIA or minor stroke in previous 3 months	low dose aspirin placebo	2.7 years	0.84 (0.65 - 1.08)	38 (16 - 85)
4S [7]	4444 patients 35 - 70 years angina or MI cholesterol 5.5-8.0 mmol/L	simvastatin placebo	5.4 years	0.64 (0.47 - 0.88)	65 (38 - 224)
ESPS2 [9]	6602 patients >18 years TIA or stroke in previous 3 months	aspirin dipyridamole aspirin plus dipyridamole placebo	2 years	0.82 (0.69 - 0.97) 0.84 (0.71 - 1.00) 0.63 (0.52 - 0.76)	37 (20 - 319) 42 (21 - >1000) 18 (13 - 29)

ANYONE FOR TENNIS ELBOW?

Tennis elbow is common, 4-7 per thousand per year in general practice, according to a Dutch systematic review of injection treatment [1]. Peak incidence is between 35 and 54 years, and only 5% are due to wielding a racket in anger. They estimate that on average the problem lasts for between 6 months and 2 years, and in Holland between 10 and 30% of patients take time off work with their tennis elbow, and the average time-off is 12 weeks.

Lack of elbow grease

The three commonest remedies used by Dutch GPs are analgesics (18-35%), steroid injections (14-38%) and physiotherapy (28-30%).

The obvious advantages of injection are that the patient doesn't have to take tablets, the injection is easy to do, and no referral is necessary. Incidentally Bandolier really likes

the 'how-to-do' pictures of various injection procedures in Dr Bull's book [2]. Do the injections work?

Systematic review

Twelve randomised trials were unearthed, five comparing steroid plus local anaesthetic injection with injection of local anaesthetic or saline, two comparing different steroid doses or formulations, and five comparing steroid with other treatment. The Dutch are tough reviewers, and found fault with most of the trials. They did go on to try to pool the results from the various trials.

Bandolier struggled with the validity of their analysis

the outcome of 'treatment success' taken from nine trials was necessarily crude because the different trials used different ways of measuring success

The 'does steroid injection for tennis elbow work?' vote-counting Table

Trial	dichotomous data	odds ratio significant at authors' most important follow-up time	odds ratio significant for 2-6 weeks	odds ratio significant beyond 6 weeks
Price et al 1991	Y	Y	Y	N
Day et al 1978	Y	Y	Y	n/a
Murley 1954	Y	Y	Y	n/a
Freeland & Gribble 1954	Y	N	n/a	N
Halle et al 1986	N	n/a	n/a	n/a

n/a means no data available. References are in the systematic review. Y = yes, N = no.

- 2 the real problem is that they pooled trials which compared steroid versus local anaesthetic or saline with trials which compared steroid with another active treatment, such as NSAID, wrist brace or ultrasound. Not surprisingly pooling apples with pears produced evidence of heterogeneity in the
- 3 within the trials which compared steroid versus local anaesthetic or saline there was variation in the number of injections studied

Results

Bandolier has tried to tease out the results for the trials comparing steroid with local anaesthetic or saline. The best we can do is to count votes. The disadvantage of vote-counting is that it takes no account of whether trials are big or small, no account of the extent or size of the effect found in the various trials, and no account of the relative validity of the trial designs.

So, three of four trials with available data showed an effect of steroid injection compared with local anaesthetic alone or saline at authors' most important follow-up time. Three of three showed significant short term (2-6 weeks) advantage, and none showed a long term advantage (more than 6 weeks; two trials with data).

What evidence there is, and some of it is pretty ancient, does support an effect of steroid injections, but this is not a clean answer, and the effect doesn't last for more than six weeks.

All that glisters isn't gold

The report shows how difficult it is for all of us to pick out the problems. When you read you need to have your critical faculties honed. *Bandolier* does not believe that the trials in the review should have been pooled in the way they were, and the data presented is not robust enough for us to dignify it with an NNT.

Shoulder steroid versus elbow steroid

In *Bandolier* 32 five studies comparing shoulder joint injection of steroid with local anaesthetic or saline also suggested that the steroid injections could produce no useful long term effect (NNT for success beyond four weeks from injection of 17 compared with saline, with a confidence limit which included no benefit to any patient, and for steroid versus local anaesthetic the NNT was 33).

Elbow joint injections may do better short term but don't look different from shoulder injections beyond six weeks. Once again the WD40 approach of injecting steroid is not a long term solution to the problem.

Adverse effects

The adverse effects of elbow injection in the Price trial were pain after injection in 58 of the 116 injected with steroid plus local compared with 9 of 29 with local alone, and skin atrophy in 31 of 116 compared with 5 of 29. These seem a bit high.

References

- WJ Assendelft, EM Hay, R Adshead, LM Bouter. Corticosteroid injections for lateral epicondylitis: a systematic overview. British Journal of General Practice 1996; 46:209-16.
- 2 Bull MJV, Gardiner P. Surgical procedures in primary care. Oxford: Oxford University Press, 1995.

RIGHT IN THE GUT

Bandolier has found three interesting papers on evidence in gastroenterology. One is to do with the relationship between Barrett's oesophagitis and colon cancer, and the others tell us about risks associated with endoscopy and agreement beween clinicians. One is a systematic review and the other is an audit, but they illustrate how collecting evidence informs us.

Barrett's oesophagitis and colon cancer

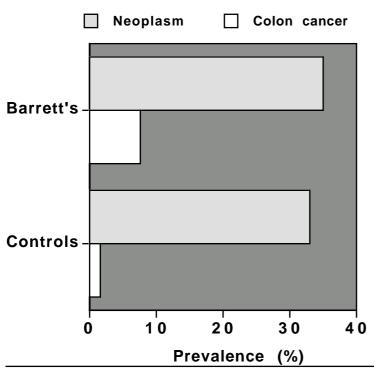
Barrett's oesophagitis is a complication of long-standing gastro-oesophageal reflux disease (GORD). Prolonged and excessive exposure of the lining of the oesophagus leads to changes in the types of cell which make up the epithelium. Instead of the usual flat, squamous, cells lining the oesophagus, columnar cells take over. This can extend from just a few centimetres from the gastro-oesophageal junction to the full length of the oesophagus.

Development of columnar epithelium is associated with an increased risk of oesophageal cancer (about 1 in 50 to 170 patient years). But a recent systematic review [1] demonstrates that patients with Barrett's oesophagitis also have an increased risk of colon cancer.

Systematic review

The authors, from South Carolina, did a search to identify papers looking at colon cancer, polyps, neoplasms or adenomas in Barrett's oesophagus. They extracted data on patients with the disorder, and on controls, and on the numbers of patients found to have colon cancer or adenomas on colonoscopy.

Prevalence of colon neoplasms (benign and malignant) and colon cancer in patients with Barrett's oesophagitis and controls



They found five uncontrolled studies, in which the prevalence of colon cancer in patients with Barrett's oesophagus was 4.6% (8/174). The prevalence of colon adenomas was 27% (36/134).

They found nine papers with control groups. In size they varied from 17 to 175 patients and found rates of colon cancer among patients with Barrett's oesophagus of 0 to 14%. Overall 52 of 685 had colon cancer, an average rate of 7.6%.

The prevalence of benign plus malignant colon neoplasms ranged between 18 and 47%. Overall 176 of 510 had colon cancer, an average rate of 35%.

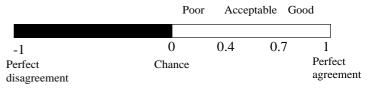
The authors also created a comparison cohort of 513 patients aged less than 80 years described in studies of colonoscopic screening for colorectal cancer. Of these 513, 8 (1.6%) had colon cancer and 169 (33%) had colon neoplasms.

So the conclusion is that while colon neoplasms occur at about the same rate in people who have and who do not have Barrett's oesophagitis, the risk of developing colon cancer is about five times greater in patients with Barrett's oesophagitis. Nearly 8% of them will have colon cancer. Is this prevalence high enough to consider screening?

Endoscopists agree with each other

Yes they do. A series of studies assessing the agreement obtained between experienced endocopists examining slides and videos, and between experienced and training endoscopists looking at slides, agreement was acceptable to excellent for identification of important features like mucosal breaks and complications of reflux disease [2]. Values for kappa (*Bandolier* 37) were in the range 0.5 to 0.9.

Kappa



Endoscopy safety

Risks are usually associated with therapy - some rare but severe adverse effect, for instance. But a prospective audit of endoscopy done in the UK gives us an insight into the risks of diagnosis. Not just having a diagnosis which could change your life, but the risk of the test itself.

A prospective audit of 13,036 diagnostic and 1,116 therapeutic upper gastrointestinal endoscopies were audited in the North West region and East Anglia [3]. There were 104 deaths within 30 days of the procedure. Some died as a result of perforation, but in many cases the relationship with endoscopy was debatable. For instance, deaths due to pneumonia, infarct and cerebrovascular accident often occurred in sick, elderly patients.

The conservative estimate was that in the 13,036 patients undergoing diagnostic endoscopy there were seven endoscopy-related deaths, or 1 in 2,000. The authors thought that this might be an under-estimate.

This is a thorough audit, well reported and with a host of details. It draws attention to ways in which things can be made as safe as possible, and to the appropriate guidelines.

References:

- 1 CW Howden, CA Hornung. A systematic review of the association between Barrett's esophagus and colon neoplasms. American Journal of Gastroenterology. 1995 90:1814-9.
- 2 D Armstrong et al. The endoscopic assessment of esophagitis: a progress report on observer agreement. Gastroenterology 1996 111:85-92.
- MA Quine, GD Bell, RF McCloy, JE Charlton, HB Devlin, A Hopkins. Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing, and sedation methods. Gut 1995 36:462-7.

Doing the right test right

Bandolier is constantly on watch for examples of benefits from doing the right thing in the right way - of getting evidence into practice. So we were delighted when we found an example which brought this together with another theme of diagnostic tests.

Maastricht experiment

No, not something to do with politics, but an experiment conducted with 85 GPs serving a population of 187,000 around this delightful little town [1]. What they did, starting in 1985, was to arrange with local laboratories to provide written feedback twice a year to individual GPs on test ordering and appropriateness of tests requested. They used guidelines from their regional health authority and Dutch College of General Practitioners. Comparison was made with other practices which did not have the feedback.

Outcomes

These were the numbers of tests done each year from 1983 to 1991, together with their costs. The costs of tests for the tests practices were measured against a 7% annual incremental trend and control laboratories.

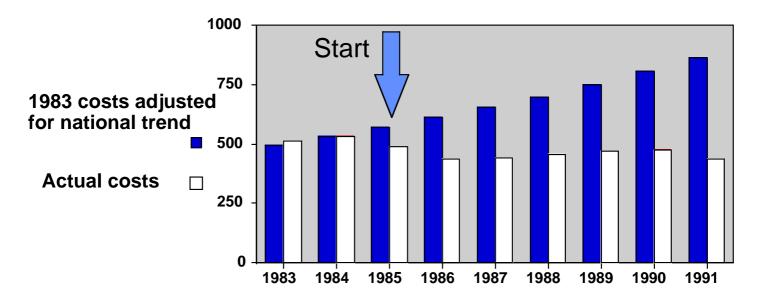
Results

Costs in the trial practices for all the laboratory tests, including ECGs and radiology actually started falling after the first year. In control practices and laboratories, the costs rose inexorably. These cost changes derived from really large differences in test requesting. Comparing 1991 with 1985, the change in test requesting by the 85 GPs was:

Haematology	-39%
Serology	-60%
Clinical chemistry	-30%
Urine/faeces	-48%
Bacteriology/virology	-17%
ECG/X-ray/histology	0%
Endoscopy	+260%
	,

Because of the rising rate of requesting generally, but the falling trend by the GPs receiving feedback, the cost differential rose each year. By 1991 the test practices were saving just under \$400,000 for their 187,000 population - about \$2 a year for each person - taking into account the cost of providing the feed-back service.

Variable costs for all tests except endoscopy \$,000

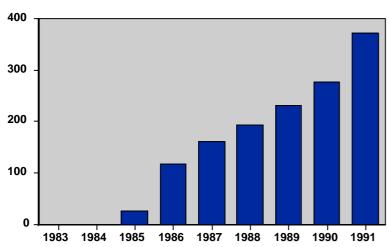


Comment

We should not be surprised at this. Audit Commission Reports showed large reductions in X-ray referrals following the introduction of guidelines (see *Bandolier* 12), and a randomised controlled trial of introducing radiology guidelines showed significantly more referrals were appropriate, together with some fall in total request [2].

Laboratories trying to cope with ever increasing request load would probably appreciate the breather they would get if schemes like this were introduced. The money saved in the Maastricht experiment was not insignificant - just try multiplying £1.50 by the population of a GP practice, of a health authority, or a nation.

Annual savings above national trend \$,000



Getting on with it

When we know that doing something can produce major savings, and provide a better and more appropriate service without any restriction on anyone's freedom, what stops us from getting on and doing it? Answers on a postcard. Here is just one bit of information, which should not be squirrelled away. Any Chief Knowledge Officer worth his or her salt would be trumpeting this abroad and making sure something was done.

At the very least it would be worth a "fact-finding visit" to see how the Dutch did it (and this group continues to publish useful and interesting stuff). Maastricht is a delightful city, with great hospitals, and close to the beautiful ancient capital of the Frankish Empire - Charlemagne's tomb in Aachen is awesome.

References:

- 1 RAG Winkens et al. Routine individual feedback on requests for diagnostic tests: an economic evaluation. Medical Decision Making 1996 16: 309-14
- 2 P Oakeshott, SM Kerry, JE Williams. Randomized controlled trial of the effect of the Royal College of Radiologists' guidelines on general practitioners' referrals for radiographic examination. British Journal of General Practice 1994 44: 197-200.

NHS Executive - Northern and Yorkshire Regional Office Research and Development Directorate

CALL FOR PROPOSALS

Research and Development Primary Care Scheme

The R&D Primary Care Scheme aims to provide an infrastructure which encourages and enables NHS practitioners to conduct high quality research and development in the primary care setting, with relevance to improving health and health care. It is designed to support practices in which

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The selection criteria include the practice and individual's commitment to networking, the research experience of the applicant, training and development issues and practice resource requirements. They are detailed in a specification document which is available from the NYRO R&D Directorate's offices.

Informal enquiries may be made to Mr Tony James, Regional R&D Manager (0191 301 1332), or Mr Paul Henderson, R&D Support Manager (0191 301 1330), from whom an application pack can be obtained. You are strongly advised to contact your local Primary Care Research Network; contact details are contained in the application pack. Written enquiries and completed forms should, however, be addressed to:

Mr Paul Henderson

NHS Executive Northern and Yorkshire Regional Office Research and Development Directorate John Snow House Durham University Science Park DURHAM DH1 3YG

Please note that the closing date for applications is 1 August 1997. Interviews will be held on 4 September 1997.

FOR N&Y ONLY

LAW OF DIMINISHING RETURNS

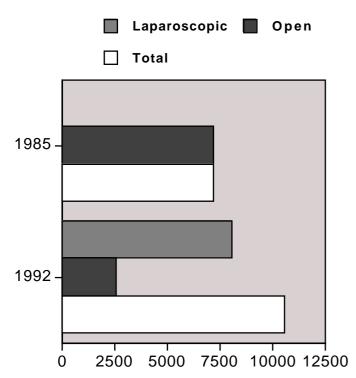
The effects of medical progress are subtle and complex. A fascinating paper from Maryland shows just how complex.

The march of the laparoscope

Laparoscopic cholecystectomy has made dramatic inroads into conventional surgical practice, with many benefits. A large survey of discharge data from all 54 acute care hospitals in Maryland was carried out between 1985 and 1992 to identify open and laparoscopic cholecystectomies [1].

The annual rate increased from 1.7 per 1000 residents in 1987-9 to 2.2 per 1000 residents in 1992, an increase of 28%. Patients undergoing laparoscopic cholecystectomy were younger, less likely to have acute cholecystitis or a commonduct stone, and were more likely to be white and have private health insurance.

Total cholecystectomies in Maryland



Operative mortality

Operative mortality of laparoscopic cholecystectomy was less than that for the open operation (odds ratio 0.22; 95% confidence interval 0.13 to 0.37). There was a decline in the overall cholecystectomy mortality rate from 0.84% in 1989 to 0.56% in 1992.

Swings and roundabouts

When a new medical or surgical advance is introduced, it may be used not simply for the population that received the old treatment, but for a new population. This may be because it is safer (as is the case for laparoscopic cholecystectomy), or because it is more acceptable to patients (as with MRI rather than myleography, for instance).

The authors' conclusions were striking. What they found was "although the adoption of laparoscopic cholecystectomy has been accompanied by a 33% decrease in overall operative mortality per procedure, the total number of cholecystectomy-related deaths has not fallen because of a 28% increase in the total rate of cholecystectomy."

The authors are duly cautious, and the paper is worth reading for its careful analysis of possible confounding factors. But one is left with the uneasy suspicion that the development of a new technology to solve an old problem has led to a new population being treated whose need for, and benefit from, treatment is not as clearly defined.

Bandolier does not like to appear Luddite. Laparoscopic cholecystectomy is clearly an important advance (though not all keyhole surgery has fulfilled its early promise), but the subtle change in threshold that takes place on introduction of a new technology is always a cause for concern.

1 CA Steiner et al. Surgical rates and operative mortality for open and laparoscopic cholecystectomy in Maryland. New England Journal of Medicine 1994 330: 403-8.

6TH UK WORKSHOP ON TEACHING EVIDENCE-BASED MEDICINE

Chair: Professor DL Sackett

6-11 July 1997; Oxford, UK

This workshop is designed to help clinicians and others who are already familiar with EBM to dvelop skills in teaching EBM in clinical and classroom settings. A limited number of places may be available for those who want to become familiar with Evidence-Based Health Care. Application forms from:

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